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LEYDIG, VOIT & MAYER
350 CAMBRIDGE AVENUE
SUITE 200
PALO ALTO, CA 94306

EXAMINER	
MARKS, M	
ART UNIT	PAPER NUMBER
185	5

DATE MAILED: 11/29/88

This is a communication from the examiner in charge of your application

COMMISSIONER OF PATENTS AND TRADEMARKS

[X] This application has been examined [ ] Responsive to communication filed on _____ [ ] This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. [X] Notice of References Cited by Examiner, PTO-892.
2. [X] Notice re Patent Drawing, PTO-948.
3. [ ] Notice of Art Cited by Applicant, PTO-1449
4. [ ] Notice of Informal Patent Application, Form PTO-152
5. [ ] Information on How to Effect Drawing Changes, PTO-1474
6. [X] PTOL-413

Part II SUMMARY OF ACTION

1. [ ] Claims 1-30 are pending in the application.
   Of the above, claims 1-13 are withdrawn from consideration.
2. [ ] Claims _____ have been cancelled.
3. [ ] Claims _____ are allowed.
4. [ ] Claims 14-30 are rejected.
5. [ ] Claims _____ are objected to.
6. [ ] Claims 1-38 are subject to restriction or election requirement.
7. [ ] This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.
8. [ ] Allowable subject matter having been indicated, formal drawings are required in response to this Office action.
9. [ ] The corrected or substitute drawings have been received on _____. These drawings are [ ] acceptable; [ ] not acceptable (see explanation).
10. [ ] The [ ] proposed drawing correction and/or the [ ] proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been [ ] approved by the examiner. [ ] disapproved by the examiner (see explanation).
11. [ ] The proposed drawing correction, filed _____, has been [ ] approved. [ ] disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.
12. [ ] Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has [ ] been received [ ] not been received [ ] been filed in parent application, serial no. _____; filed on _____.
13. [ ] Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. [ ] Other

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-13, drawn to chimeric receptors, classified in Class 530, subclass 387.

II. Claims 14-38, drawn to the DNA, mammalian cell line and methods of preparing the receptor, classified in Class 435, subclass 70 and 172.3+.

The inventions are distinct, each from the other because of the following reasons:

Inventions [Group II] and [Group I] are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different products or (2) that the product as claimed can be made by another and materially different process (MPEP 806.05(f)). In the instant case the product as claimed can be made by another and materially different process such as protein synthesis.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Bertan Rawland on October 4, 1988 a provisional election was made with traverse to prosecute the invention of Group II,claims 14-38. Affirmation of this election must be made by applicant in responding to this office action. Claims 1-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 14-38 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to DNA constructs for expression of a chimeric polypeptide which is a subunit of an immunoglobulin molecule. See MPEP 706.03(n) and 706.03(z).

Subunits of other multi-unit receptors were not enabled (eg. IgE receptors, IL-1 and IL-2 receptors, fibronectin receptors and other integrins). It would require undo experimentation to determine the variable and constant region amino acid and genomic sequence homolgies of these receptors for use in cross- species chimeric constructions.

Claims 14, 28, 33, and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14, 28 and 36 are indefinite by claiming constructs

for a multi-unit receptor, cells, and a method for expressing a multi-unit receptor. Not all multi-unit receptors are taught in the instant invention. Is immunoglobulin intended rather than the genus multi-unit receptor? If not, which multi-unit receptor is intended (eg. an integrin, an IL-1 or IL-2 receptor, or an IgE receptor)? Binding activities are associated with numerous multi-chain polypeptides (ie. receptor). Please clarify what is intended by the multi-unit receptor.

Claims 28 and 33 are confusing and obscuring in the recitation " a mammalian cell having first and second DNA constructs for expression of different first and second subunits... each of said first and second constructs comprising...". Since the first and second constructs are comprised of the same components, they may be one in the same. Wording such as "a mammalian cell having <u>different</u> first and second DNA constructs..." would clarify this claim.

Claims 25-27 are rejected under 35 U.S.C. 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 25 refers to a promoter in claims 15 or 16 while no promoter is specifically mentioned in either claim 15 or 16. Claims 26 and 27 fail to further define claims 14-16 by including an additional element (ie. a replication system).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless-

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

A person shall be entitled to a patent unless

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-34 and 36 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cabilly (L).

Cabilly teaches various DNA constructs for the expression of chimeric immunoglobulin heavy chains, chimeric immunoglobulin light chains, chimeric immunoglobulins, and chimeric immunoglobulin fragments (ie. chimeric subunits of a multiunit receptor). Cabilly teaches various expression vectors for use in either prokaryotic or eukaryotic host cells (See page 15 lines 6-29). Cabilly also teaches the use of eukaryotic host cells, including various mammalian cell types (page 18 line 6-34 and page 19 lines 1-8). Further, Cabilly teaches the use of the regulatory elements required for expression in vertebrate cells (page 18, lines 11-14). Finally Cabilly teaches the coexpression of both the heavy and light chains of immunoglobulin in the same host (page 23 line 29-30). Thus, all aspects of the instant invention, except for expression specifically in murine myeloma

cells, was taught by Cabilly.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office Action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 35, 37-38 are rejected under 35 U.S.C. 103 as being unpatentable over Cabilly(L).

Cabilly teaches the use of eukaryotic host cells , including vertebrate cell hosts (pages 18 and 19). In the absence of unexpected results, it would be obvious to use myeloma cells as a type of mammalian cell as taught by Cabilly. It would be particularly obvious to use myeloma cells to express a DNA construct whose major regulatory and coding sequences are endogenous to said myeloma cell, since the endogenous host would contain the both 1) the trans-acting factors necessary for activating immunoglobulin cis elements and 2) the cytoplasmic organelles and enzymes required for co- and post-translational

processing of immunoglobulin chains.

Claims 14-38 are rejected under 35 U.S.C. 103 as being unpatentable over Gillies (S) as applied to claims 35, 37 and 38 above, and further in view of Cabilly (L).

Cabilly is applied as described above. It would be obvious to use mammalian cells, particularly myeloma cells, to express a chimeric polypeptide whose components are endogenous to said myeloma cells. Gillies teaches the use of mammalian cells (ie. myeloma cells) as well as the method for expressing immunoglobulin genes in myeloma cells. In the absence of unexpected results, it would be obvious to one of ordinary skill in the art to utilize the vector and cells of Gillies to express the chimeric constructs of Cabilly in order to produce the chimeric receptor (ie. antibody or immunoglobulin fragment) of Cabilly.

Please note the following references as being pertinent to the state of the art: Murphy (M), Seno(T), and Dolby (U).

Any inquiry concerning this communication should be directed to Examiner Michelle Marks, Ph.D. at telephone number 703-557-0664.

11.2.88 msm